AF

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/015,387	12/12/2001	Kevin P. Baker	39780-2830.054 US	9861

35489 7590 12/02/2005

HELLER EHRMAN LLP
275 MIDDLEFIELD ROAD
MENLO PARK, CA 94025-3506

EXAMINER	
FREDMAN, JEFFREY NORMAN	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 12/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/015,387
Filing Date: December 12, 2001
Appellant(s): BAKER ET AL.

Barrie D. Greene
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed September 12, 2005 appealing from the Office action mailed January 18, 2005.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

There are currently no related appeals and interferences.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

No evidence is relied upon by the examiner in the rejection of the claims under appeal.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 112 – Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 28-32 and 44-52 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species situations that "Satisfactory disclosure of a ``representative number'' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.)

All of the current claims encompass a genus of nucleic acids which are different from those disclosed in the specification, since the claims are not limited to any particular SEQ ID NO, but are open to a nucleic acid that ranges from 80% to 99% identical to SEQ ID NO: 219, without any guidance on conserved portions of the protein

structure. Further, the claims encompass "hybridization" language without any correlative function as required by the utility guidelines.

Most significantly, the genus includes variants for which no written description is provided in the specification. This large genus is represented in the specification by only the particularly named SEQ ID No 219. Thus, applicant has express possession of only one particular nucleic acid sequence in a genus which comprises hundreds of millions of different possibilities. Here, no common element or attributes of the sequences are disclosed, not even the presence of certain domains.

There is no showing or evidence which links structural limitations or requirements to any particular functional limitations. Further, these claims encompass alternately spliced versions of the nucleic acids, allelic variants including insertions and mutations, nucleic acids which encode inactive precursor proteins which have a removable amino terminal end, and only specific nucleic and amino acid sequences have been provided. No written description of alleles, of upstream or downstream regions containing additional sequence, or of alternative splice variants has been provided in the specification.

It is noted in the recently decided case The Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997) decision by the CAFC that

> "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See Fiers, 984 F.2d at 1169- 71, 25 USPQ2d at 1605- 06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may

> achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372- 73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. "

In the current situation, the definition of the nucleic acids as having 80%-99% sequence identity to SEQ ID NO: 219 lacks any specific structure, since it lacks the correlation between structure and function that is at the heart of the caselaw and of the written description guidelines.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

The current situation is a definition of the compound without identifying the structure function relationship of the compound, so that the compound is claimed solely its nucleic acid sequence related 80%-99% to SEQ ID NO: 219 without any correlative function to delimit the structure.

In the instant application, certain specific SEQ ID NOs are described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention,

with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any nucleic acids other than those expressly disclosed which comprise SEQ ID NO 219. Therefore, the claims fail to meet the written description requirement by encompassing sequences which are not described in the specification.

(10) Response to Argument

The issue is whether the claims comply with the written description requirement of 35 U.S.C. 112, first paragraph. In this analysis, Appellant attempts to address the structure function issue by adding the function "wherein the encoded polypeptide induces proliferation of kidney mesangial cells". This function has literally nothing to do with structure whatsoever. Appellant also fails to note that a "representative number of species" is required. This is considered by the USPTO written description guidelines which note that in an unpredictable art, a single species is not sufficient to describe the genus.

It is the absence of any real structure function relationship and the absence of a representative number of species which supports the conclusion that there is insufficient descriptive support for the current claims. This argument rests on several grounds. First, the single sequence that is actually described is not representative of the genus of any sequence which shares the percent identity under the stated conditions. Second, the claims entirely lack a structure function relationship since the function given has no

ability to limit the genus of polypeptides. Third, the claim encompasses species other than human.

Absence of a representative number of species

In the current case, the first question is what constitutes a generic claim. The genus of polypeptides represents every possible variation which could occur in SEQ ID Nos: 220, that has 80% identity. Appellant attempts to delimit this number by arguing that the claims is limited to functional variants. However, Appellant does not provide any description of which changes will be functional and which will not, so this subgenus is entirely undefined. For the 603 nucleotides which encode this protein of 201 amino acids, 20% variation permits a change of 120 nucleotides. In order to provide a representative number of species, in a genus which contains literally 4^{120} (or written out fully, approximately 176,684,706,477,838,430,000,000,000,000,000,000,000,000,000,000,000,000,000,000,000,000,000,000,000,000,000,000) different members, the court in Lilly required "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. (Lilly at page 1406)." (As a side comment, the genus size here is larger than that at issue in Deuel). Lilly continues to note that in other cases, two chemical compounds in a subgenus were insufficient to describe that genus. In the current case, Appellant argues that the single species of a single SEQ ID NO is sufficient to describe 4^{120} other sequences for which no description whatsoever is

given. These sequences may be of any size or structure, so long as they are 80% identical. Appellant's analysis is flawed since there is no expectation in the instant case of insubstantial variation because the functional limitation devolves solely to the ability of the protein to induce proliferation of kidney mesangial cells. However, this induction is entirely unrelated to the structure of the protein. The function provides absolutely no guidance or information regarding the structure and does not delimit the structure in even the smallest or most miniscule possible way. So the argument by Appellant that there would be insubstantial variation is not correct since the function of overexpression does not limit the protein in any significant way.

Appellant appears to also be making the argument that the size of the genus is not relevant. This is not found persuasive because the size of the genus is a central issue. If the genus were small, a written description rejection would be less likely, since the examples would be more representative of the genus. Here, where the genus includes 176,684,706,477,838,430,000,000,000,000,000,000,000,000,000,000,000,000,000,000,000,000,000,000 different members, none of which are disclosed or taught by Appellant, the argument that the demonstrated species is representative is not found persuasive.

Absence of any structure-function relationship

Second, when Appellant relies upon the analysis of the written description guidelines, this analysis is based upon the assumption that there will be insubstantial

variation, as noted in many of the examples including example 9. Appellant states that it is not clear where the requirement for a structure function relationship arises. In Lilly, the Federal Circuit notes that "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is." This shows that function alone is insufficient. However, Appellant's analysis is flawed since there is no expectation in the instant case of insubstantial variation because the functional limitation devolves solely to the ability of the protein to induce proliferation of kidney mesangial cells. This is not like example 9, where the functional limitation involved a protein which retained adenylate cyclase activity. In the example 9 case, the argument of insubstantial variation was that there was an expectation that stringently hybridizing proteins which retained the specific function of stimulating adenylate cyclase would differ insubstantially. Appellant's fundamental position fails to equate with the written description guidelines because in the guidelines, there is function correlated to the structure. The function in Appellant's claims, however, lack any association with the structure of the protein whatsoever. So consonant with the case law in Lilly, Enzo and the other written description decision of the Federal Circuit, it is clear that the current claims fail to meet the written description requirement because there is no structure function relationship which limits the genus size. The guidelines require more. They require a structure function relationship.

The claim scope broadly encompasses sequences from other species

Finally, when Appellant argues that the case is different from the issues cited in Lilly and Fiers, Appellant fails to appreciate the breadth of the claim. The current claim

clearly reads on sequences found not only in humans, but in other species. This was the crux of the decision in Lilly, that a rat insulin sequence did not provide sufficient breadth to provide descriptive support for a claim which encompassed human insulin nucleic acid sequences. Appellant's claim suffers from the same flaw, since the claim would clearly encompass sequences from other species. For example, an alignment of nucleotides 103-942 of SEQ ID NO: 219 with the mouse Genbank Accession No. NM 175631 shows an 81% alignment (with one region having an 89% alignment). (This is post filing date art). So the claim as written would encompass an mouse sequence, not described by Appellant, which is the express problem raised in Lilly. It is clear that Appellant did not have possession of this sequence, since there was no recognition of the particular changes that would result in the sequence. (see alignment below).

```
>gi|28274689|ref|NM_175631.1|  GU Mus musculus cerebellin 4 precursor protein (Cbln4), mRNA
          Length = 2802

 Score =  628 bits (317), Expect = e-176
 Identities = 485/541 (81%)
 Strand = Plus / Plus

Query: 103  gttctgcatgagctccttaaaggacaaaggtaacagagccagcgagagagctcgagggga 162
            ||||||||||||||||||||||||||||||||||||||||||||||||  ||  || |||| ||||
Sbjct: 937  gttctgcatgagctccttaaaggacaaaggtaacagagccagccagccagttcgaaggga 996


Query: 163  gactttgacttcaagccacagaattggtggaagtgtgcgcgccgccgccgccgtcgc--- 219
            |||      ||||  ||  ||||||||||||||| |||||||| || |||| |||
Sbjct: 997  gac------ttcagtcctgagaattggtggaagtgcgcgcgccgctgctgccgccgccac 1050


Query: 220  ------tcctgcagcgctgtcgacctagccgctagcatcttcccgagcaccgggatcccg 273
                 ||||||||||||||||| |||||| || || |||||||||| || ||||||||
Sbjct: 1051 cgctgttcctgcagcgctgtcgatctagccactggcgtcttcccgagctcccggatcccg 1110


Query: 274  gggtaggaggcgacgcgggcgagcaccagcgccagccggctgcggc-tgcccacacggct 332
            |||||| ||||| |||  | |||||  |||||||   |||||| || ||| ||| |||||
Sbjct: 1111 gggtagcaggcgccgcctgggagcagaagcgcca---ggctgccgcttgcgcacgcggct 1167


Query: 333  caccatgggctccgggcgccgggcgctgtccgcggtgccggccgtgctgctg 384
            |||||||||||||| ||||||||||||||||| ||| || ||||| ||||||
Sbjct: 1168 caccatgggctccgcgcgccgggcgctgtccgtggtaccagccgttctgctg 1219


Query: 402  gctgcccgtctgggcacagaacgacacggagcccatcgtgctggagggcaagtgtctggt 461
```

```
            |||||| |||||||||||||| |||||||| || ||||| ||||||||||||||||||||
Sbjct: 1228 gctgcctgtctgggcacagaatgacacggaaccgatcgttctggagggcaagtgtctggt 1287


Query: 462  ggtgtgcgactcgaacccggccacggactccaagggctcctcttcctccccgctggggat 521
            |||||||||||||||||| || || |||||||||| || || || ||||| ||||||||
Sbjct: 1288 ggtgtgcgactcgaacccagctacagactccaagggatcatcatcttcccctctggggat 1347


Query: 522  atcggtccgggcggccaactccaaggtcgccttctcggcggtgcggagcaccaaccacga 581
            |||||||||||| || |||||||||| || || |||||||| ||||||||||||||||||
Sbjct: 1348 atcggtccgggcagcaaactccaaggtggctttttcggcggttcggagcaccaaccacga 1407


Query: 582  gccatccgagatgagcaacaagacgcgcatcatttacttcgatcagatcctggtgaatgt 641
            |||||| |||||||||||||||| |||||||||||||| |||||||||||||| || ||
Sbjct: 1408 gccatctgagatgagcaacaagactcgcatcatttactttgatcagatcctggttaacgt 1467


Query: 642  gggtaatttttttcacattggagtctgtctttgtagcaccaagaaaaggaatttacagttt 701
            |||||||||||||||||||| |||||||||| ||||| || |||||||| || |||||
Sbjct: 1468 gggtaatttttttcacattggaatctgtctttgtggcaccgaggaaaggaatctatagttt 1527


Query: 702  cagttttcacgtgattaaagtctaccagagccaaactatccaggttaacttgatgttaaa 761
            |||||||||||| |||||||||||||||||||||| ||||||||||||||||||||||
Sbjct: 1528 cagttttcacgtaattaaagtctaccagagccaaaccatccaggttaacttgatgttaaa 1587


Query: 762  tggaaaaccagtaatatctgcctttgcgggggacaaagatgttactcgtgaagctgccac 821
            |||||||||||| || ||||| ||||| || || |||||||| || |||||||| |||||
Sbjct: 1588 tggaaaaccagtcatctctgcatttgctggtgataaagatgtgacccgtgaagccgccac 1647


Query: 822  gaatggtgtcctgctctacctagataaagaggataaggtttacctaaaactggagaaagg 881
             ||||| || || || ||||| || ||||| |||||||| ||||||||||||||||||||
Sbjct: 1648 taatggagtgctcctgtacctggacaaagaagataaggtctacctaaaactggagaaagg 1707


Query: 882  taatttggttggaggctggcagtattccacgttttctggctttctggtgttccccctata 941
            ||| ||| | || ||||||||||||||||||||||||||||||||||||| || |||||
Sbjct: 1708 taacttgctcggtggctggcagtattccacgttttctggctttctggtgtttcctctata 1767


Query: 942  g 942
            |
Sbjct: 1768 g 1768
```

So the claims clearly encompass sequences which were neither taught nor described by the current specification.

Appellant makes the specific argument that highly conserved sequences would have more difficulty in meeting the written description standard and Appellant argues that this result would be perverse. To the contrary, this would be the desired result and is the result dictated by the Federal Circuit. If the Federal Circuit in Lilly wished, they

could have granted the patent and given the patentee control over both rat and human insulin when only rat insulin was disclosed.

The decisional law in this area has been very consistent. The Federal Circuit in Lilly, Fiers, Rochester and many other cases has determined that the written description issue applies to situations where the definition of the subject matter of the claims fails to provide description commensurate with the genus. The most recent caselaw directly supports this rejection. As the District Court in University of Rochester v. G.D. Searle & Co., Inc. (2003 WL 759719 W.D.N.Y.,2003. March 5, 2003.) noted "In effect, then, the '850 patent claims a method that cannot be practiced until one discovers a compound that was not in the possession of, or known to, the inventors themselves. Putting the claimed method into practice awaited someone actually discovering a necessary component of the invention." This is similar to the current case since the breadth of the current invention claims comprise compounds which were not in the possession of, or known to the inventors. In a genus that is literally incalculably immense, the specification shows one embodiment.

The claims include a single species which is not representative of the full scope of the genus. The guidelines support the rejection, particularly the requirement of Example 9 for a structure function relationship. Therefore, the written description rejection is maintained.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

JEFFREY FREDMAN
PRIMARY EXAMINER
11/19/05

Conferees:

Gary Benzion

SPE 1637

GARY BENZION, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Gary Jones

SPE 1634

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600